cultured in absence of exogenously added IL-2, TNF-α and/or IFN-γ.

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 1-45 are in this case. Claims 22-45 were withdrawn under a restriction requirement as drawn to a non-elected invention. Claims 1-21 have been rejected. Claims 6, 8 and 18 have now been canceled. Claims 1 and 12 have now been amended. New claims 46 and 47 have now been added.

35 U.S.C. § 112, First Paragraph, Rejections

The Examiner has rejected claims 1-5, 10-17 and 20-21 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, has possession of the claimed invention. The Examiner's rejections are respectfully traversed. Claims 1, 10, 12 and 20 have now been amended.

In particular, the Examiner points out that Applicant is not in the possession of the claimed invention since the specification fails to define all growth conditions suitable for enhancing veto activity in any HPC cells.

In the interest of expediting prosecution in this case, Applicant has elected to amend independent claims 1 and 12 to include the limitations of claims 6 and 18 (respectively) thereby overcoming Examiners rejections with respect to these claims and any claims dependent therefrom.

In view of these amendments, Applicant believes to have overcome the 35 U.S.C. § 112, first paragraph, rejections.

35 U.S.C. § 112, Second Paragraph, Rejections

The Examiner has rejected claims 8, 10, 18 and 20 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiners rejections are respectfully traversed. Claims 8 and 18 have now been canceled, rendering moot the Examiner's rejection. Claims 10 and 20 have now been amended per Examiner's suggestion.

35 U.S.C. § 103(a) Rejections - U.S. Pat. No. 5,806,529 in view of Bachar-Lustig et al. or Mobest et al. or Vavrova et al.

The Examiner has rejected claims 1-21 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Pat. No. 5,806,529 in view of Bachar-Lustig et al. or Mobest et al. or Vavrova et al.

The Examiner states that the '529 patent teaches a method of inducing tolerance to a transplant by administration of HPCs cells. The Examiner further states that the '529 patent does not teach that the HPCs are cultured ex-vivo under conditions suitable for inducing or enhancing veto activity, but that such conditions are taught by Bachar-Lustig et al., Mobest et al. or Vavrova et al. As such, the Examiner concludes that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Bachar-Lustig et al., Mobest et al. or Vavrova et al. to those of the '529 patent to obtain the claimed invention.

Applicant disagrees with examiners assertion that one of ordinary skill in the art would have been motivated to combine the teachings of Bachar-Lustig et al., Mobest et al. or Vavrova et al. to those of the '529 patent to obtain the claimed invention.

Prior to the finding presented in the instant application, the veto activity of myeloid differentiated HPCs was not known. The present inventor has shown for the first time, that culturing under the conditions taught in the instant application enables generation of a veto cell preparation which possesses up to 80-fold more total veto activity than that possessed by the total number of primary non-cultured HPCs which can be harvested from a human donor employing state-of-the-art techniques.

Thus, the present invention, provides for the first time, the motivation to use such cultured HPCs in transplantation.

Although the prior art cited by the Examiner describes culturing methods with which expansion of HPCs can be effected, these prior art studies do not describe or even suggest the use of expanded HPC cultures in transplantation nor do they recognize the veto activity inherent to myeloid differentiated HPCs.

Thus, Applicant is of the opinion that the teachings of Bachar-Lustig et al., Mobest et al. or Vavrova et al. would not motivate one of ordinary skill in the art to modify the method described in the '529 patent to include myeloid differentiated HPCs. Further evidence for this lack of motivation comes from the fact that in the time period between publication of the '529 patent and filing of the instant application (approximately 3 years), no study contemplated or attempted to combine HPC culturing methodology (available since 1997, Mobest et al.) with transplantation as described in the '529 patent, thereby demonstrating that the prior art cited by the Examiner does not provide sufficient motivation to make the present invention.

Notwithstanding from the above, Applicant has elected to introduce limitations which are directed at the preferred culturing methodology of the present invention. Thus, New claims 46 and 47 which dependent from claims 1 and 12 (respectively) further define the culturing conditions to that devoid of

exogenously added IL-2, TNF-α and/or IFN-γ. Support for such claim limitations can be found throughout the instant specification.

Such culturing condition are neither taught nor are they suggested by the prior art cited by the Examiner. In fact, the prior art cited by the Examiner teaches away in describing culturing conditions which include the above described cytokines (see for example, Abstract of Vavrova et al.)

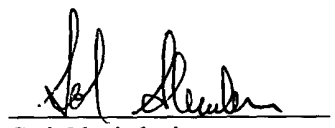
As is described in the instant application:

> "culturing of HPCs according to the present invention is effected in the presence of factors inducing myeloid differentiation and in the absence of cytokines such as IL-2, TNF-α and IFN-γ or of any form of antigenic stimulation. This ensures that any contaminating T lymphocytes, being non-stimulated, will not survive the culture conditions and thus will not contaminate the cultured HPC preparation utilized by the method of the present invention" (page 27, lines 12-19)

such culturing conditions provide numerous benefits for transplantation since they ensure that the administered cells are free of CTLs and as such incapable of inducing graft versus host disease (GVHD) in the recipient.

In view of the above amendments and remarks it is respectfully submitted that claims 1-5, 7, 9-17 and 19-21 and New claims 46-47 are now in condition for allowance. Prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,



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Date: March 18, 2003.

VERSION WITH MARKING TO SHOW CHANGES MADE

In the Claims:

1. (Amended) A method of inducing tolerance to a transplant transplanted from a donor to a recipient, the method comprising:

(a) culturing an HPC population under growth conditions suitable for inducing myeloid differentiation~~suitable for inducing or enhancing veto activity in at least a portion of said HPC population~~, thereby generating a tolerance-inducing cell population; and

(b) administering a dose of said tolerance-inducing cell population prior to, concomitantly with or following transplantation of the transplant, thereby inducing tolerance to the transplant in the recipient.

10. (Amended) The method of claim 1, wherein said veto activity is enhanced ~~per~~ in each cell ~~in~~ of said HPC population.

12. (Amended) A method of transplanting a transplant derived from a donor to a recipient, the method comprising:

(a) administering to the recipient a dose of cultured HPCs, cultured under conditions suitable for inducing myeloid differentiation, said cultured HPCs having enhanced veto activity as compared to non-cultured HPCs; and

(b) transplanting the transplant to the recipient.

20. (Amended) The method of claim 12, wherein said enhanced veto activity is enhanced ~~per~~ in each cell ~~in~~ of said cultured HPCs.

46. (New) The method of claim 1, wherein said culturing said HPC population is effected in absence of exogenously added IL-2, TNF-α and/or IFN-γ.

47. (New) The method of claim 12, wherein said cultured HPCs are cultured in absence of exogenously added IL-2, TNF-α and/or IFN-γ.